

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
22 February 2001 (22.02.2001)

PCT

(10) International Publication Number
WO 01/12575 A1(51) International Patent Classification⁷: C07B 59/00,
C07D 209/48, C07C 211/03, G01N 33/58(74) Agent: BRANTS, Johan, Philippe, Emile; De Clercq,
Brants & Partners cv, E. Gevaertdreef 10 A, B-9830 Sint-
Martens-Latem (BE).

(21) International Application Number: PCT/EP00/04632

(22) International Filing Date: 22 May 2000 (22.05.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
99870172.6 11 August 1999 (11.08.1999) EP(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).(71) Applicant (*for all designated States except US*): UNIVER-
SITE CATHOLIQUE DE LOUVAIN [BE/BE]; Place De
L'Université 1, B-1348 Louvain-la-Neuve (BE).**Published:**

— With international search report.

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): MARCHAND,
Jacqueline [BE/BE]; Rue Du Basson 48, B-6001
Marcinelle (BE). GREGOIRE, Vincent [BE/BE]; Rue
Du Fond Marie Monseu 17, B-1330 Rixensart (BE).*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*(54) Title: METHODS FOR PREPARING PERFLUORINATED [¹⁸F]-RADIOLABELLED NITROIMIDAZOLE DERIVATIVES
FOR CELLULAR HYPOXIA DETECTION(57) Abstract: The present invention relates to chemical synthesis of radiolabelled perfluorinated bioactive compounds. More particularly, the present invention relates to radiolabelled compounds to be used as indicators for tissue hypoxia. More particularly, the present invention relates to the synthesis and the use of [¹⁸F] labelled perfluorinated nitroimidazole compounds having an incorporation of [¹⁸F] atoms characterized by a specific radioactivity of the compound comprised between 1 and 30 Ci/mmol, preferably between 1 and 20 Ci/mmol, preferably 1 and 10 Ci/mmol. More particularly to [¹⁸F] labelled EF3 or [¹⁸F] labelled EF5. The present invention also relates to a method for the detection of tissue hypoxia in a patient comprising introducing an [¹⁸F] labelled nitroimidazole compound into said patient, imaging tissue hypoxia in said patient, and, quantifying tissue hypoxia in said patient.

WO 01/12575 A1